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09/829,563	04/11/2001	Jack V. Smith		7743

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EXAMINER

BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 08/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/829,563	Applicant(s) Smith
Examiner Mauri Garcia Baker, Ph. D.	Art Unit 1627

-- The MAILING DATE of this communication appars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on Jun 4, 2002

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 1035 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-7 is/are pending in the application.

4a) Of the above, claim(s) 5 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-4, 6, and 7 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 4) Interview Summary (PTO-413) Paper No(s). _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

DETAILED ACTION

1. The Response filed June 4, 2002 (Paper No. 3) is acknowledged. No claims were amended, added or cancelled. Therefore, claims 1-7 are pending.

Election/Restriction

2. Applicant's election of species with traverse is also acknowledged. The type of indicator elected was NAD and the type of "analyte of interest" elected was prostate specific antigen.

3. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Applicant has elected prostate specific antigen (PSA) as the "analyte of interest". PSA is a protein. Instant claim 5 recites "wherein said target compound is not a protein". Although claim 5 lacks antecedent basis for the phrase "target compound", the examiner has interpreted this to be equivalent to the "analyte of interest" in claim 1. Thus, as the "analyte of interest" is elected to be PSA, a protein, claim 5 is directed to a non-elected species.

5. Claim 5 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

6. Please note MPEP § 803.02 with respect to species elections:

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

7. Thus, claims 1-4, 6 and 7 are under examination.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for analytes and indicators therefor that are art standard, does not reasonably provide enablement for any indicator and any analyte. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is clear from applicant's specification how one might practice this invention with specific analytes and indicators therefor that are art standard; however, there is insufficient guidance as to how to carry out the claimed method using any indicator and any analyte. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to a "method for detecting an analyte of interest" by identifying a nucleounit that binds the analyte and then conjugating the nucleounit to an "indicator for the analyte of interest". Importantly, defendant claims 2 and 7 recite an enormous variety of indicators and analytes of interest. This represents extremely broad scope. Also, claim 7 recites a very diverse Markush group of analytes of interest where many of the analytes are ill

defined, for example, “complement components”, “gold”, “nitrogen”, “nonprotein nitrogen”, “blood”, “vitamins”, “HIV” and the various “autoimmune diseases” set forth on page 119 of the claims.

(3 and 5) The state of the prior art and the level of predictability in the art: Methods for making and using synthetic nucleic acid ligands to various analytes were known in the art at the time of filing (see art rejections below); however, the art uses established techniques (such as radiolabeling or fluorescent labeling) that are compatible with the analyte being interrogated. The invention is such that the indicator and analyte must be compatible, i.e. the analyte must be able to be detected using the indicator-nucleounit conjugate. One of ordinary skill would not be able to guess, *a priori*, how to carry out the claimed method using any indicator and any analyte (i.e. those set forth in claims 2 and 7) as the method of detecting for each would be different (involves different chemistry). Claim 7 recites a very diverse Markush group of analytes of interest and finding indicators to work with any and all such analytes would be highly unpredictable. Applicant’s claimed scope of indicator and analyte entities represents only an invitation to experiment regarding possible compatible detection schemes.

(4) The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. Such persons of ordinary skill in this art, given its unpredictability, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

(6-7) The amount of direction provided by the inventor and the existence of working examples: The specification gives no guidance to permit one of skill in the art to devise compatible detection schemes for any indicator or analyte as claimed. The examples are unclear as to the mechanism for detection and only provide a small subset of examples that cover the scope of the claimed indicators and analytes. Specifically, *the instant specification fails to identify that structure which is required for the claimed activity.*

Please also see rejection under 35 USC 112, second paragraph below.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification gives one skilled in the art no indication of how to carry out the full scope of the claimed method when any indicator or analyte is used. The instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the full scope of the claimed invention. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The claims recite a method “for detecting an analyte of interest” that uses a nucleounit indicator conjugate. It is simply unclear as to how the “indicator for the analyte of interest” is determined (i.e. instant step b) in claim 1). The dependent claims recite a list of various indicators and analytes (i.e. instant claims 2 & 7) but it is unclear how each of the indicators relate to each of the analytes. Can they all be used interchangeably? This creates a great deal of confusion. See also rejection under 35 USC 112, first paragraph above.

B. Claim 4 recites “wherein said nucleounit is not a nucleic acid ligand”. This limitation renders the claim indefinite as it is unclear as to applicant’s intent. This is because the term “nucleic acid ligand” is not defined. In a broad sense, a “nucleic acid ligand” could be any nucleic acid that binds to a ligand. The creation of such “ligands” appears to be the goal of step a) of applicants method and thus claim 4 is very confusing.

C. Claim 6 appears to be a duplicate of claim 1 as claim 1 does not require that the nucleounit indicator conjugate is bound to a solid support either. Or, one could consider

claim 6 as failing to further limit the subject matter of previous claim 1. These problems render the claim indefinite and highly confusing.

D. Claim 7 recites a very diverse Markush group of analytes of interest where many of the analytes are ill defined, for example, “complement components”, “gold”, “nitrogen”, “nonprotein nitrogen”, “blood”, “vitamins”, “HIV” and the various “autoimmune diseases” set forth on page 119 of the claims. These entries render the claim indefinite as it is unclear as to the definitions of each of these analytes. Moreover, the various “autoimmune diseases” set forth on page 119 of the claims are not set forth in correct Markush group format, which also brings confusion to the claim.

E. Claim 7 also recites “but not limited to the following:” (page 119 of the claims). The phrase renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

13. Claims 1, 3, 4, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Gold et al (US 5,270,163).

Gold et al disclose a method for creating “high affinity nucleic acid ligands that specifically bind a desired target” by a procedure called SELEX (see column 1, lines 17-25). The high affinity nucleic acid ligands of Gold et al may be used in “assay methods” and “diagnostic procedures” (see column 1, lines 25-29). Gold et al disclose a variety of possible target molecules, see column 1, lines 31-35. The reference discloses that “[m]ost proteins or small molecules are not known to specifically bind to nucleic acids (see column 1, lines 38-39; also column 8, lines 40-49) reading on the limitations of instant claim 4. Specifically, randomized oligonucleotides are generated, screened and partitioned, and the ligands that bind are amplified via PCR (see column 5, line 40 through column 6, line 31; also, for example, column 11, line 5). Various buffers are used in the process, such as citrate (column 26, lines 3-6), reading on instant claim 3. Gold et al disclose carrying out the SELEX process on various targets, such as insulin (see Example 6 in column 46) reading on the specific “analyte of interest” in claim 7.

14. Claims 1, 4, 6 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Heilig et al (US 6,376,474).

Heilig et al disclose a method for using the SELEX procedure to identify "high affinity nucleic acid ligands to complex tissue targets" (see Abstract). The SELEX procedure is the same as disclosed in Gold et al (US 5,270,163) and this patent and an entire family of "SELEX Patent Applications" is described, disclosed and incorporated by reference (see column 1, line 34 through column 3, line 8). Thus the disclosure of the method steps would be the same as set forth in the rejection above. The reference specifically describes "oligonucleotide ligands with high specificity for particular tumor antigens could become as important as monoclonal antibodies for the detection, imaging and surveillance of cancer" (column 15, lines 33-36). The reference specifically discloses making a ligand to PSA (column 15, lines 42-45).

15. Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Cubicciotti (US 6,287,765).

Cubicciotti disclose methods for making and selecting synthetic nucleotides (see Abstract). These molecules are called "aptamers", see discussion in column 91, line 18 through column 92, line 26. Specifically, randomized oligonucleotides are generated, screened and partitioned, and the ligands that bind are amplified via PCR (see, for example, patented claims; column 3, line 27 through column 4, line 3; column 79, lines 25-47; and column 84, line 50 through column 85, line 65). Cubicciotti discloses the

creation of conjugates with various indicators, see column 17, line 57 though column 20, line 22. The reference specifically discloses indicators reading on claim 2 (and specifically the elected species of NAD), see Example 4 in columns 191-194 and Example 5 in columns 194-199. The reference also teaches using various targets reading on those of instant claim 7, see e.g. Examples 4 and 5. The elected species of PSA is specifically disclosed in Example 14 (columns 215-219), as well as buffers that read on those claimed. Solution and solid phase methods are disclosed (see, for example, column 219, lines 25-55).

Status of Claims/Conclusion

16. No claims are allowed.
17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.
18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (703) 308-4537. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to

the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
August 22, 2002



MAURIE GARCIA BAKER, Ph.D.
PATENT EXAMINER